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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,902	07/03/2003	Hiroshi Takeyama	Q76104	8672
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SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037			EXAMINER GRAFFEO, MICHEL	
			ART UNIT	PAPER NUMBER
			1614	

DATE MAILED: 08/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/611,902

Applicant(s)

TAKEYAMA ET AL.

Examiner

Michel Graffeo

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 April 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4,6,7,16 and 17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4,6,7,16 and 17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Status of Action

Claims 1-4, 6-7 and 16-17 are examined.

Applicant has amended claims 4, 7 and 16-17, canceled claims 5 and 8-15 and provided arguments for the patentability of claims 1-4, 6-7 and 16-17 in the response filed 14 April 2006.

Applicant's arguments, see response, filed 14 April 2006, have been fully considered and are persuasive to the extent that the rejection over Bessette (WO 00/33857) under 35 USC §102, is withdrawn. However, in light of the amended claims the rejection under 35 USC §103 is maintained and based on a new reference. Any rejection not specifically stated in this Office Action has been withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 102

1) Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by "The antitumor effect to stomach cancer by benzyl alcohol," Meeting of Japan Surgical Society on April 12-14, 2000, issued on March 10, 2000, PP-1457 (listed on PTO Form

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1449, dated 27 October 2003, with a translation provided by Applicant), hereafter referred to as "Reference PP-1457."

Reference PP-1457 teaches that benzyl alcohol induced cell death by apoptosis in stomach cancer cells (in the cell line STKM) thereby anticipating current claims 1-3.

In reference to the limitation in instant claims 2 and 8 of "external administering," adding the benzyl alcohol to the cultured cells in their dish would include externally administering the composition; in other words, the reference does disclose direct injection of the benzyl alcohol directly into the cells. The reference also indicated:

~~Since we found out that Benzyl alcohol had antitumor effect to a stomach cancer, we report said effect herein.~~

which, absent factual evidence to the contrary would have been *in vivo* and since the gut space is "external" to the body, would have been anticipated as a method of external administration.

2) Claims 1-3 are rejected under 35 U.S.C. 102(a) as being anticipated by "The antitumor effect of benzyl alcohol against breast cancer," The 10th Annual Meeting of the Japanese Breast Cancer Society, July 5-6, 2002, B-323 (listed on PTO Form 1449, dated 27 October 2003, with a translation provided by Applicant), hereafter referred to as Reference B-323.

Reference B-323 benzyl alcohol induced cell death in breast cancer cells (in cell lines BSMZ and MCF-7). The reference also teaches that according to the apoptosis examination, Caspase-3 and 8 was "admitted in MCF-7" but not in the BSMZ cell line.

In reference to the limitation in instant claim 8 of "external administrating," adding the benzyl alcohol to the cultured cells in their dish would include externally administering the composition; in other words, the reference does disclose direct injection of the benzyl alcohol into the individual cells and the specification does not define "external administration".

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4) Claims 1-4, 6-7 and 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6284786 to Casciari et al. in view of "The antitumor effect to stomach cancer by benzyl alcohol," Meeting of Japan Surgical Society on April 12-14, 2000, issued on March 10, 2000, PP-1457 (listed on PTO Form 1449, dated 27 October 2003, with a translation provided by Applicant), hereafter referred to as

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"Reference PP-1457." in light of *Stedman's Medical Dictionary*, 25th Edition (1990), p. 1026-1027 (cited for definition purposes).

Casciari et al. teach that vitamin C has anticancer properties in breast cancer for example (see col 3 lines 50-52).

Reference PP-1457 teaches that benzyl alcohol induced cell death by apoptosis in stomach cancer cells (in the cell line STKM).

Stedman's defines necrosis as "pathological death of one or more cells...resulting from irreversible damage" (p. 1026). Thus, absent any factual evidence to the contrary, the cell death occurring in the treatment methods of the prior art would be considered necrosis, according to the common medical definition by Stedman's, therefore meeting the limitation of "necrosis".

In addition, the following case law is believed to be relevant to the instant claim rejections:

In re Kerkhoven (205 USPQ 1069, CCPA 1980) states that "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the same purpose: the idea of combining them flows logically from their having been individually taught in the prior art." Therefore, would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine vitamin C and benzyl alcohol, motivated by their having been taught by the prior art to be useful in treating cancerous tumors, consonant with the reasoning of the cited case law.

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Pertinent Art:

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

- Fukuda T, et al., "Anti-tumor promoting effect of glycosides from *Prunus persica* seeds," February 1, 2003 *Biol. Pharm. Bull.* 26(2): pages 271-273. The reference teaches anti-tumor activity of benzyl alcohol derivatives in carcinogenesis on mouse skin.
- Barrett et al. (US Patents 6,492,363 and 6,310,060) teach benzyl alcohol derivatives for the treatment of various proliferative diseases, including various cancers.
- Ohmori et al. (US Patent 5,431,925) teaches a nutrient composition for patients being treated with anti-cancer agents containing vitamins and minerals, including vitamin C, as one of the major components (see abstract and claim 1).
- Jamison, JM, et al., "Autoschizis : a novel cell death," 2002 *Biochemical Pharmacology* 63: 1773-1783. The reference teaches that tumor cells are seen undergo necrosis, apoptosis and autoschizis all at once (p. 1775). The reference also defines autoschizis as a type of necrosis and that it may compliment apoptosis in antitumor activity (abstract & p. 1775).

Response to Arguments - 35 USC § 102

Applicant's arguments filed 14 April 2006 have been fully considered and are persuasive for reasons of record with respect to the Bessette (WO 00/33857) reference.

Response to Arguments - 35 USC § 102

Applicant's arguments filed 14 April 2006 have been fully considered but they are not persuasive with respect to the PP-1457 and B-323 references. Applicant's argue that the references do not disclose that the BA induces tumor cell death via necrosis. Products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art

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teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. To that extent, a teaching of the same administration of the same agent must result in the same effects regardless if such an effect is reported. Moreover, Stedman's Dictionary defines necrosis as "pathological death of one or more cells...resulting from irreversible damage" (p. 1026). Thus, absent any factual evidence to the contrary, the cell death occurring in the treatment methods of the prior art would be considered necrosis, according to the common medical definition by Stedman's, therefore meeting the limitation of "necrosis".

Response to Arguments - 35 USC § 103

Applicant's arguments filed 14 April 2006 have been fully considered but they are not persuasive. The response is directed to claims comprising the limitation of heparin in lieu of vitamin C. The presently filed claims under examination do not contain the limitation of a composition comprising heparin. For this reason, the arguments are not applicable to the instant Office Action.

Response to Arguments - 35 USC § 112

Applicant's arguments filed 14 April 2006 have been fully considered and are persuasive for reasons of record.

Conclusion

No claim is allowed.

Applicant's amendment, the addition of the limitation vitamin C, necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michel Graffeo whose telephone number is 571-272-8505. The examiner can normally be reached on 9am to 5:30pm Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

14 August 2006

MG

Ardin H. Marschel 8/17/06

**ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER**